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MANUSCRIPT

Abstract

Objectives

European guidelines state left ventricular (LV) end-diastolic wall thickness (EDWT) $\geq 15\text{mm}$ suggests hypertrophic cardiomyopathy (HCM), but distinguishing from hypertensive heart disease (HHD) is challenging. We identify cardiac magnetic resonance (CMR) predictors of HHD over HCM when EDWT $\geq 15\text{mm}$.

Methods

2481 consecutive clinical CMRs between 2014-15 were reviewed. 464 segments from 29 HCM subjects with EDWT $\geq 15\text{mm}$ but without other cardiac abnormality, hypertension or renal impairment were analyzed. 432 segments from 27 HHD subjects with EDWT $\geq 15\text{mm}$ but without concomitant cardiac pathology were analyzed. Magnitude and location of maximal EDWT, presence of late gadolinium enhancement (LGE), LV asymmetry (>1.5 -fold opposing segment) and systolic anterior motion of the mitral valve (SAM) were measured. Multivariate logistic regression was performed. Significance was defined as $P < 0.05$.

Results

HHD and HCM cohorts were age-/gender-matched. HHD had significantly increased indexed LV mass ($110 \pm 27\text{g/m}^2$ vs $91 \pm 31\text{g/m}^2$, $P = 0.016$) but no difference in site or magnitude of maximal EDWT. Mid-wall LGE was significantly more prevalent in HCM. Elevated indexed LVM, mid-wall LGE and absence of SAM were significant multivariate predictors of HHD, but LV asymmetry was not.

Conclusions

Increased Indexed LV mass, mid-wall LGE and absence of SAM are better CMR discriminators of HHD from HCM than EDWT ≥ 15 mm.

Key words

Hypertension; Cardiomyopathy, Hypertrophic; Hypertrophy, Left Ventricular;
Magnetic Resonance Imaging; Cardiac Imaging Techniques

Key points

- Hypertrophic cardiomyopathy (HCM) is often diagnosed with end-diastolic wall thickness ≥ 15 mm.
- Hypertensive heart disease (HHD) can be difficult to distinguish from HCM.
- Retrospective case-control study showed that location and magnitude of EDWT are poor discriminators.
- Increased left ventricular mass, systolic anterior motion of the mitral valve and mid-wall fibrosis are independent predictors of HHD.
- Cardiac magnetic resonance parameters facilitate a better discrimination between HHD and HCM.

Abbreviations

ESC	-	European Society of Cardiology
HCM	-	Hypertrophic cardiomyopathy
LV	-	Left ventricular
EDWT	-	End-diastolic wall thickness
HHD	-	Hypertensive heart disease
CMR	-	Cardiovascular magnetic resonance imaging
LVH	-	Left ventricular hypertrophy
SAM	-	Systolic anterior motion of the mitral valve / sub-valvular apparatus
eGFR	-	Estimated glomerular filtration rate
SCD	-	Sudden cardiac death
SSFP	-	Steady state free precession
BSA	-	Body surface area
RV	-	Right ventricular
EDV	-	End-diastolic volume
ESV	-	End-systolic volume
SV	-	Stroke volume
EF	-	Ejection fraction
M/V	-	Mass to volume ratio
LGE	-	Late gadolinium enhancement

INTRODUCTION

The 2014 European Society of Cardiology (ESC) guidelines on hypertrophic cardiomyopathy (HCM) advocate that this condition should be considered when left ventricular (LV) end-diastolic wall thickness (EDWT) measures $\geq 15\text{mm}$ in ≥ 1 myocardial segments, measured by any imaging technique[1]. Furthermore, according to the 2011 American College of Cardiology Foundation / American Heart Association guidelines, HCM is usually recognized by regional LV wall thickness $\geq 15\text{mm}$, with measurements of 13-14mm considered borderline[2]. Therefore, the pattern and degree of wall thickening are considered important in establishing a diagnosis of HCM. Concomitant abnormal loading conditions may confound the wall thickness cut-off. Concentric patterns of wall thickening are commonly thought to be associated with hypertension, the most common cause of increased afterload. However, asymmetric patterns of LV thickening have been described in hypertensive heart disease (HHD) with 2D echocardiography[3]. Cardiovascular magnetic resonance imaging (CMR) is currently non-invasive gold-standard for assessing LV mass, volume and EDWT[4][5]. The role of CMR in suspected HCM is recognized in International guidelines[1][6] and it is gaining an increasing role in certain hypertensive individuals[7]. Patients with suspected HCM and/or hypertension are increasingly being referred for CMR to attempt to distinguish between the two pathologies. To date, studies that have compared CMR findings in hypertension and HCM were either in subjects who fulfilled echocardiographic criteria for left ventricular hypertrophy (LVH)[8] or CMR criteria for LVH[9]. Wall thicknesses up to 20mm have been described in previous CMR studies in hypertension[10], so being

able to distinguish HHD and HCM where EDWT is $\geq 15\text{mm}$ is important and, to date, not previously investigated. Consequently, the aims of this study were to compare age- and sex-matched subjects with HHD with subjects with HCM where EDWT $\geq 15\text{mm}$ in both cohorts using a comprehensive multi-parametric CMR protocol. We sought to identify which CMR imaging findings can serve as discriminators between these two pathologies. We aimed to assess location and magnitude of hypertrophy, myocardial replacement fibrosis and ancillary imaging findings, such as systolic anterior motion of the mitral valve/sub-valvular apparatus (SAM) and aortoseptal angulation which have been described as markers of HCM[11].

MATERIALS AND METHODS

Hypertrophic cardiomyopathy study population

This was a retrospective observational study from a prospectively maintained clinical CMR database of consecutive adult patients (>18 years old) referred for clinical CMR. Retrospective analysis of anonymized routine clinical data was confirmed to be in accordance with the NHS Health Research Authority guidelines for NHS research ethics approval. Subjects provided written consent for their CMR data to be used for post-hoc research. The diagnosis of HCM was based on the clinical information and CMR imaging findings of a non-dilated, hyper-dynamic hypertrophied LV in the absence of cardiac or systemic disease that could result in similar magnitude of hypertrophy, in a method previously described[9]. All patients with HCM had an expressed LV phenotype permitting an unequivocal diagnosis in the clinical context. Endomyocardial biopsy and/or genetic testing was not used to reach the diagnosis[12]. A total of 2481 CMR performed between 1st January and 31st

December 2014 were reviewed. Subjects without a diagnosis of HCM were excluded. Of those with a diagnosis of HCM and regional EDWT $\geq 15\text{mm}$ in ≥ 1 segment, those with apical only HCM, evidence of previous myocardial infarction, moderate-severe valvular heart disease and arterial hypertension (including elevated office blood pressure or on anti-hypertensive medications) were excluded. A severely decreased estimated glomerular filtration rate (eGFR) $< 30\text{ml/min/1.73m}^2$ was also an exclusion criterion, resulting in a final sample size of 464 myocardial segments from 29 consecutive patients (**Figure 1A**). Medical records were reviewed for documented symptoms of heart failure, arrhythmia and family history of HCM, sudden cardiac death (SCD) or arrhythmia.

Hypertensive heart disease study population

150 patients with confirmed arterial hypertension were recruited from the Bristol Heart Institute tertiary hypertension clinic between February 2012 and April 2015. Subjects provided written consent. Baseline demographic and clinical characteristics were recorded. Hypertensive subjects with any concomitant myocardial pathology that may confound the hypertrophic response, e.g. moderate-severe valvular heart disease, acquired or inherited cardiomyopathy and suspected athlete's heart, were excluded. An eGFR $< 30\text{ml/min/1.73m}^2$ was also an exclusion criterion. Hypertensive subjects with HHD with EDWT $< 15\text{mm}$ were also excluded. The final hypertensive sample size was 432 myocardial segments from 27 patients (**Figure 1B**). Medical records were reviewed for documented symptoms of heart failure, arrhythmia and family history of HCM, SCD or arrhythmia.

CMR protocol

All CMRs were performed at 1.5T (Avanto, Siemens, Erlangen, Germany). Steady state free precession (SSFP) short axis whole LV cines (8mm slice thickness, no slice gap, temporal resolution 38.1ms, echo time 1.07ms, representative field of view in-plane pixel size 1.5 x 0.8 mm) were used for the estimation of end-diastolic LV mass and LV volumes, which were then indexed to body surface area (BSA), as previously described[13]. Previously validated[14] threshold-detection software (CMR42, Circle Cardiovascular Imaging Inc., Calgary, Canada) was used to include papillary muscles and LV trabeculae to be included in LV mass estimation in accordance with the latest Society for Cardiovascular Magnetic Resonance imaging guidelines[15]. Papillary muscles and trabeculae were then included in the blood pool volume for assessment of end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and ejection fraction (EF), as described previously[13]. The LV mass/volume ratio (M/V), CMR equivalent of the echocardiogram-derived relative wall thickness measurement, was derived by dividing LV mass by EDV[16, 17].

Average global longitudinal strain from 4-chamber and 2-chamber SSFP cines was measured with voxel-tracking post-processing software (TissueTracking, CVI42, Circle Cardiovascular Imaging Inc, Calgary). The presence of LV crypts, defined as previous as discrete approximately V- or U-shaped extensions of the blood signal, considered on cine viewing to penetrate >50% of the thickness of adjoining compact myocardium in diastole[18], was assessed visually. The presence of LV non-compaction / hypertrabeculation was deemed present when the ratio of non-compacted to compacted myocardium was >2.3 at end-diastole as previously

described[19]. All aforementioned CMR measurements and analyzes were performed by an experienced CMR reader blinded to the clinical details.

Segmental end-diastolic wall thickness

LV wall thickness was measured from the short-axis cines at end-diastole using pixel-wise analysis (CMR42, Circle Cardiovascular Imaging Inc., Calgary, Canada). Briefly, endocardial and epicardial contours were defined, excluding right ventricular (RV) marginal septal trabeculations and LV papillary muscles and trabeculae. The automated software then mapped 100 cords, each perpendicular to the LV wall, per end-diastolic slice (**Figure 2Aii and 2Bii**). American Heart Association 16-segment model was generated automatically, using manually positioned anterior and inferior RV insertion points as reference markers. EDWT was defined as the mean thickness for each myocardial segment. Such measurements from short-axis cine CMR images have been demonstrated to result in good inter and intra-observer variability[20]. Asymmetrical segmental EDWT was defined as EDWT >1.5-fold the EDWT of the opposing segment, as previously described[21]. EDWT measurements were performed by an experienced CMR reader blinded to the clinical details and other CMR findings.

Systolic anterior motion of the mitral valve / sub-valvular apparatus

As previously described[11], systolic anterior motion of mitral valve (SAM) was defined as: i) partial when the mitral valve leaflets and/or chordae moved towards the ventricular septum but without direct contact during systole, as assessed on the 3-chamber long-axis and short-axis cine stack, and ii) complete when there was

contact. The presence or absence of SAM was based on analysis of 2 independent CMR readers, with a consensus reading in cases of discrepancy.

Aortoseptal angulation

The aortoseptal angle was defined as the angle, on 3-chamber long-axis cine at end-systole, between a line drawn along the right side of the interventricular septum (parallel to the proximal right ventricular endocardial border), and a line drawn through the long axis of the aortic root, where a value of 180° would be a straight line from septum to aorta and reducing values representing increased angulation, as previously described [11] (**Figure 3**). Aortoseptal angle measurements were performed by an experienced CMR reader, blinded to all other CMR and clinical data.

Myocardial replacement fibrosis

Myocardial replacement fibrosis was assessed by late gadolinium enhancement (LGE)[22]. An inversion-recovery fast gradient echo sequence performed, in two phase-encoding directions where required due to artifact, was performed 10-15 minutes after intravenous administration of 0.1mmol/kg gadobutrol (Gadovist, Bayer Pharma AG, Germany). Tailored inversion times were used in each patient to achieve myocardial nulling. LGE presence and location were analyzed visually by 2 independent experienced CMR readers, blinded to the clinical and hypertrophy data.

The segmental distribution of LGE, including LGE at anterior/inferior basal/mid RV insertion points was recorded. Discrepancies were resolved by consensus.

Statistical analysis

Statistical analysis was performed using SPSS Version 21 (Armonk, NY, USA: IBM Corp). Normally distributed continuous variables were expressed as mean \pm standard deviation and compared using unpaired Student's T test. Non-parametric data were compared with Mann-Whitney U test. Categorical variables were expressed as percentages and analysed using the Fisher's exact test. Univariate and multivariate logistic regression analysis was performed to identify predictors of HHD compared to HCM. Significance was set at two-sided $P < 0.05$.

RESULTS

Demographics

Demographic data are displayed in **Table 1**. The HHD and HCM were matched in age (57 ± 13 years vs 62 ± 10 years, $P = 0.166$) and sex (74% male vs 59% male, $P = 0.268$).

Subjects with HHD had significantly higher body mass index ($33 \pm 5 \text{ kg/m}^2$ vs $29 \pm 5 \text{ kg/m}^2$, $P = 0.003$). Symptoms of arrhythmia and family history of SCD or arrhythmia were significantly more common in HCM compared to HHD. Within the hypertensive cohort, the mean office systolic blood pressure was $178 \pm 31 \text{ mmHg}$ and the mean office diastolic blood pressure was $98 \pm 15 \text{ mmHg}$. Grading of blood pressure severity by 2013 ESH/ESC guidelines[7] was as follows: 7% *controlled* (SBP $< 140 \text{ mmHg}$ and DBP $< 90 \text{ mmHg}$), 15% *Grade 1* (SBP 140-159 mmHg and/or DBP 90-99 mmHg), 11% *Grade 2* (SBP 160-179 mmHg and/or DBP 100-109 mmHg), 48% *Grade 3* (SBP $\geq 180 \text{ mmHg}$ and/or DBP $\geq 110 \text{ mmHg}$) and 19% *isolated systolic hypertension* (SBP $> 140 \text{ mmHg}$ and DBP $< 90 \text{ mmHg}$).

Left ventricular mass

There was a significantly higher absolute LV mass in HHD compared to HCM ($240\pm69\text{g}$ vs $175\pm64\text{g}$, $P<0.0001$). There remained a significant difference when absolute LV mass was indexed to BSA (HHD: $110\pm27\text{g}/\text{m}^2$ vs HCM: $91\pm31\text{g}/\text{m}^2$, $P=0.016$). Due to the higher BMI in HHD, post-hoc analysis indexing LV mass to height^{1.7} was also performed. This allometric scaling method has recently been demonstrated to better account for obesity related increases in LV mass[23], and the significant difference persisted overall (HHD: $93\pm24\text{g}/\text{m}^{1.7}$ vs HCM: $74\pm30\text{g}/\text{m}^{1.7}$, $P=0.008$), and for female subjects (HHD: $76\pm16\text{g}/\text{m}^{1.7}$ vs HCM: $57\pm11\text{g}/\text{m}^{1.7}$, $P=0.010$) but only a non-significant trend for male subjects (HHD: $99\pm23\text{g}/\text{m}^{1.7}$ vs HCM: $84\pm33\text{g}/\text{m}^{1.7}$, $P=0.108$).

Magnitude and location of segmental EDWT

Representative examples of subjects with HHD and HCM are demonstrated in **Figure 2**. The mean maximal EDWT thickness was not significantly different between HHD and HCM ($16.9\pm1.5\text{mm}$ vs $17.5\pm2.9\text{mm}$, $P=0.988$)(**Table 2**). In both cohorts, the basal anteroseptum (segment 2) was most likely to have EDWT $\geq 15\text{mm}$ (**Figure 4A**). There was no significant difference in the number of segments with EDWT $\geq 15\text{mm}$ per patient (HDD: 2.9 ± 2.5 segments vs HCM: 2.6 ± 2.1 segments, $P=0.761$). However, the basal and mid anterolateral and inferolateral, as well as all the apical segments, demonstrated significantly thicker EDWT in HHD compared to HCM (**Table 3**). Correspondingly, LV asymmetry was significantly more common in HCM than HHD, but nevertheless asymmetry still occurred in a large minority of HHD subjects (HCM asymmetry: 90% vs HHD asymmetry: 40%, $P<0.0001$).

Replacement fibrosis

The location of mid-wall late gadolinium enhancement is demonstrated in **Figure 4B**.

LGE was significantly more common in HCM than HHD in the basal anteroseptum (38% vs 4%, $P=0.003$), the mid inferoseptum (24% vs 0%, $P=0.011$) and all the RV insertion points (basal anterior RV insertion $P<0.0001$, basal inferior RV insertion $P<0.0001$, mid anterior RV insertion $P=0.002$, mid inferior RV insertion $P=0.015$).

Similar significant differences were demonstrated in subgroup analysis of LGE in segments with EDWT ≥ 15 mm (**Figure 4C**).

Ancillary CMR findings

Complete SAM was common in HCM and absent in HHD (41% vs 0%, $P<0.0001$) (**Table 2**). There were no significant differences either in the prevalence of partial SAM (HCM: 31% vs HHD: 11%, $P=0.083$) or in the mean aortoseptal angle (HCM: $113\pm 10^\circ$ vs $115\pm 10^\circ$, $P=0.481$). LV crypts were more common in HCM than HHD (HCM: 13% vs HHD: 0%, $P=0.05$) but no cases of HHD or HCM met the criteria for LV non-compaction/hypertrabeculation.

Predictors of HHD

In univariate analysis, increasing BMI, LV mass indexed to BSA, absence of EDWT asymmetry, absence of SAM (partial or complete) and absence of mid-wall LGE were all significant predictors of HHD (**Table 4**). However, only increasing indexed LV mass, absence of SAM and absence of mid-wall LGE remained significant predictors in the multivariate logistic regression statistical model (**Table 4**). In area under the receiver operator curve analysis, indexed LV mass performed favorably at detecting HHD

(0.705 [0.567 – 0.843], $P < 0.05$). An indexed LV mass threshold of 132g/m² identified HHD over HCM with 93% specificity and 22% sensitivity (**Figure 5**).

DISCUSSION

This is the first study to investigate a comprehensive panel of multi-parametric CMR imaging findings as discriminators of hypertensive heart disease over hypertrophic cardiomyopathy when end-diastolic wall thickness, as measured by semi-automated pixel-wise CMR analysis, is ≥ 15 mm in a total of 896 myocardial segments from age- and sex-matched cohorts. We show that the magnitude (both in terms of mean maximal EDWT and number of segments with EDWT ≥ 15 mm) and location of wall thickening are not useful discriminators between HHD and HCM in this context. Furthermore, LV asymmetry, although significantly more common in HCM than HHD, was not a significant independent predictor of HCM in multivariate analysis. However, increasing LV mass indexed to BSA, the absence of SAM and the absence of myocardial replacement fibrosis were significant independent predictors of HHD in the multivariate logistic regression model.

LV mass and location/magnitude of LV wall thickening

There are conflicting results in the literature regarding the usefulness of LV mass at distinguishing HHD from HCM. Sipola et al. concluded that LV mass indexed to BSA was not useful at distinguishing 24 subjects with HCM from 94 subjects with mild-moderate hypertension[24]. Puntmann et al. showed that LV mass indexed to BSA was significantly higher in 43 HCM subjects compared to 39 subjects with treated essential hypertension [9]. Rudolph et al. found no significant difference in LV mass

indexed to height in 36 HCM subjects compared to 26 hypertensive subjects, where all participants were drawn from a population with LVH by echocardiographic criteria[8]. Furthermore, 20% of subjects with HCM may have LV mass indexed to BSA within the normal range[25]. The heterogeneity in the literature likely relates to different study populations. In our clinically relevant cohort, where EDWT ≥ 15 mm in both HHD and HCM cohorts, we show that LV mass indexed to both height^{1.7} and BSA is significantly higher in HHD and elevated indexed LV mass is a significant predictor of HHD over HCM in multivariate analysis. Our results provide further insight into a putative reason for this. We show that HHD is a concentric LV response to the increased afterload state, with significantly thicker segments in the mid lateral wall in particular compared to HCM. This is consistent with HCM being considered a more focal sarcomeric disorder, rather than a global process. However, it is important to realize that LV asymmetry, whilst more common in HCM, was not a useful discriminator between HHD and HCM in multivariate analysis. **Asymmetric HHD is well-recognized[26]**. LV asymmetry, as defined at EDWT ≥ 15 mm and >1.5 times the opposing myocardial segment, occurred in 40% of HHD in our cohort. This is markedly higher than previous echocardiographic studies, showing a prevalence of asymmetrical septal hypertrophy of 5%[3]. The reasons for this discrepancy, again, likely relate to different study populations; unselected subjects with hypertension in the echocardiographic study compared to subjects with hypertension and HHD with EDWT ≥ 15 mm in our study. A additional explanation likely also relates to the better whole heart 3D coverage with contiguous short axis cines and better tissue contrast of CMR, facilitating the identification of endocardial contours, relative to 2D echocardiography[27]. **However, the pathophysiology of asymmetric HHD is not fully**

understood and possibly relate to the basal septum representing a site of increased wall stress in hypertension [28].

Replacement fibrosis

There are also conflicting results regarding the prevalence of myocardial replacement fibrosis between HCM and HHD. Puntmann et al. demonstrated a significantly higher global LGE score amongst HCM compared to HHD[9], whereas Rudolph et al. only demonstrated a non-significant trend towards higher prevalence of LGE in HCM (74%) than in hypertension (50%)[8]. The lack of significant difference in the latter study, likely relates to the high prevalence of LGE in their hypertensive subjects and such a higher prevalence of LGE in hypertension which has not been reproduced in subsequent studies[29]. For the first time, we show that mid-wall fibrosis is a significant discriminator between HHD and HCM in myocardial segments with EDWT ≥ 15 mm. The markedly higher prevalence of LGE in HCM to HHD is consistent with the known pathophysiological differences between these conditions. HCM is characterized by myofibril disarray associated with interspersed microfibrosis[30], whereas, hypertensive LVH is a result of hypertrophy of existing cardiomyocytes, which occurs without structural disarray. However, the absence of LGE does not equate to the absence of myocardial fibrosis. The technique of acquiring LGE images with myocardial nulling requires a region of 'normal' myocardium for the nulling reference. This technique identifies focal replacement fibrosis but may fail to demonstrate global, diffuse fibrosis. T1 mapping techniques provide pixel-wise quantification of the myocardial intra and extracellular compartments and have already demonstrated increased diffuse myocardial

interstitial fibrosis in hypertensive LVH[29][31] and these techniques may also be useful to distinguish HCM from HHD[32].

Limitations

There are several limitations of our study. The absolute numbers of subjects in our study are low. However, the study is still the only study to date to compare HHD and HCM with EDWT ≥ 15 mm, selected from a population of routine clinical CMR practice. However, analyzing each subject in a segment-wise manner significantly increased the number of data points in our study. However, the small sample size precluded further subgroup analysis to determine the length and severity of hypertension and the impact of anti-hypertensive medications on the degree of EDWT. The former may be particularly relevant as precursors of hypertensive heart phenotype have been demonstrated to be associated with increasing SBP in healthy adults[33].

An important consideration is the presence of hypertension in the HCM cohort and vice versa. In the HHD cohort, subjects with family history of HCM or sudden cardiac death were excluded. HCM subjects with documented elevated BP and controlled BP on anti-hypertensive medications were excluded.

As quantification of peak velocity in the left ventricular outflow tract (LVOT) is not a routine component of our clinical multi-parametric CMR protocol for suspected HCM, this variable, as well as inducible LVOT obstruction, were not assessed.

In our study, we investigated predictors in subjects with expressed HHD and HCM phenotypes. The lack of endomyocardial biopsy and/or genetic testing is a limitation of our study. Further work is still required to refine discriminators in subjects with more mild disease states, supported by genetic profiling. In this regard, it would be interesting to incorporate CMR T1-mapping techniques in future studies to help distinguish these subjects by potentially demonstrating more intracellular (cardiomyocyte) expansion in hypertension and more extracellular expansion in HCM.

Conclusions

Distinguishing between hypertensive heart disease (HHD) and hypertrophic cardiomyopathy (HCM) can be difficult. International guidelines advocate using a wall thickness cut-off of 15mm for HCM. Our cardiovascular magnetic resonance imaging study highlights the most useful discriminating CMR imaging findings from routine clinical multi-parametric CMR. We demonstrate that an elevated indexed LV mass, the absence of mid-wall LGE and the absence of SAM are significant independent predictors of HHD over HCM in multivariate analysis in this context. The magnitude and location of the EDWT, as well as LV asymmetry, are not significant discriminators between HHD and HCM when EDWT is ≥ 15 mm. Our results suggest that the diagnosis of HCM on the basis of wall thickness alone should be made with caution in the context of concomitant hypertension. Tissue characterization with LGE is unique to CMR and supports its extended use in cases of suspected HCM, particularly where there is concomitant hypertension.

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Conflict of interest

None.

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Table and Figure legends

Table 1: Demographic data for hypertensive heart disease and hypertrophic cardiomyopathy cohorts

Table 2: CMR data for hypertensive heart disease and hypertrophic cardiomyopathy cohorts

Table 3: Mean maximal end-diastolic wall thickness in each myocardial segment for hypertensive heart disease and hypertrophic cardiomyopathy cohorts

Table 4: Univariate and multivariate logistic regression analysis of predictors of hypertensive heart disease compared to hypertrophic cardiomyopathy

Figure 1. Flow-charts demonstrating study exclusion criteria. **A)** Hypertrophic cardiomyopathy sample size (n=29). **B)** Hypertensive heart disease sample size (n=27). *Image artifact from implantable loop recorder device precluding volumetric assessment from LV short axis stack. CMR = cardiac magnetic resonance, HCM = hypertrophic cardiomyopathy, HTN = hypertension, EDWT = end-diastolic wall thickness, MI = myocardial infarction, HCM = hypertrophic cardiomyopathy, LVNC = left ventricular non-compaction cardiomyopathy, DCM = idiopathic dilated cardiomyopathy, Mod AR = moderate aortic regurgitation, AVR = aortic valve replacement.

Figure 2. Examples of patients with end-diastolic wall thickness ≥ 15 mm. **A)** Hypertensive heart disease: i-ii) Steady state free precession (SSFP) mid short-axis cine at end-diastole with maximal asymmetric wall thickness of 15.9mm, iii)

Inversion recovery (IR-LGE) mid short-axis image showing subtle replacement fibrosis at the anterior right ventricular insertion point only (white arrow), iv) SSFP 3-chamber cine at end-systole demonstrating no systolic anterior motion of the mitral valve (SAM). **B)** Hypertrophic cardiomyopathy: i-ii) SSFP mid short-axis cine at end-diastole with maximal asymmetric wall thickness of 16.3mm, iii) IR-LGE mid short-axis image showing extensive myocardial replacement fibrosis (white arrows), iv) SSFP 3-chamber cine at end-systole demonstrating SAM and associated mitral regurgitation (white arrows).

Figure 3. Representative example of measuring the aortoseptal angle.

Figure 4. Segmental distribution of end-diastolic wall thickness (EDWT) ≥ 15 mm and prevalence of late gadolinium enhancement (LGE). **A)** American Heart Association (AHA) 16-segment plot demonstrating percentage of segments with EDWT ≥ 15 mm in i) hypertensive heart disease (HHD) and ii) hypertrophic cardiomyopathy (HCM). **B)** AHA 16-segment plot demonstrating prevalence of segmental mid-wall and right ventricular insertion point LGE in i) HHD and ii) HCM. **C)** AHA 16-segment plot demonstrating prevalence of segmental mid-wall LGE in segments with EDWT ≥ 15 mm in i) HHD and ii) HCM.

Figure 5. Receiver operating curve for indexed LV mass at detecting hypertensive heart disease compared to hypertrophic cardiomyopathy.